Remarks

Applicants have now amended claims 11, 12, 15 and 16 in order to define the extracorporeal blood treatment for which the claimed method is intended to prevent clotting as chronic, intermittent, extracorporeal blood treatment.

In the Example beginning line 3 on page 5 of the specification, the reported clinical study is performed in patients undergoing "chronic, intermittent haemodialysis." Haemodialysis is one of the uses of extracorporeal blood circuits, as listed in the first paragraph on page 3. It is also the purpose for which the method is claimed in original claim 4.

The significance of limiting the claimed method to treating patients undergoing chronic, intermittent, extracorporeal blood treatment is that these patients are subject to repeated treatment occurring at intervals dictated by the extent of their disease, such as kidney disease being treated by dialysis. The claimed dosages are the dosages required for each treatment, they are not the daily dosages recited in the Petitou reference, which are administered every day to patients undergoing treatment for thrombotic disorders.

The Examiner has referred to the first paragraph in column 5 of Petitou et al '829, where it is recited, "[f]or the treatment of venous thrombosis or for the inhibition of smooth muscle cell proliferation the compounds of the invention may be administered enterally or parenterally, and for humans preferably in a daily dosage of 0.001-10mg per kg body weight."

Petitou et al teach methods for treating thrombotic diseases using a daily administration of particular compounds. The present invention relates to preventing clotting in an extracorporeal blood circuit of a patient undergoing chronic, intermittent, extracorporeal blood treatment. These represent clinically significantly different uses, as set forth in paragraph 2 on page 1 of the present specification.

> "Blood clotting in extracorporeal blood circuits needs to be prevented. Otherwise, blood coagulation occurs as soon as blood contacts artificial surfaces. As a remedy, usually unfractionated heperain (UFH) or low molecular weight heparins (LMWH) are used as anti-coagulants. Both UFH and LMWH have an effect on several stages of the blood coagulation cascade, both inhibiting factor Xa and thrombin (factor IIa)."

In paragraph 3 on the same page it is reported that the synthetic oligosaccharides such as those used in the present invention highly selectively inhibit factor Xa via

anti-thrombin III (ATIII), but have no activity on thrombin. Thus, they do not function like the heparins conventionally used. Even so, applicants discovered that they inhibit thrombin formation in extracorporeal blood circuits.

It is submitted that the teaching of Petitou et al is clearly related to the treatment of venous thrombosis and the inhibition of smooth muscle cell proliferation. Nothing is suggested regarding coagulation induced by contact with synthetic surfaces. The ordinary practitioner would not find this disclosure to provide a reasonable assurance of success in preventing blood clotting in extracorporeal blood circuits of patients undergoing chronic, intermittent extracorporeal blood treatment.

In view of the above, with the present amendment to the claims limiting them to chronic, intermittent, extracorporeal blood treatment, it is believed that claims 11-18 are in condition for allowance. Favorable action is solicited.

Should the Examiner consider that a conference would be helpful in advancing the prosecution of this

application, she is invited to telephone Applicants' attorney at the number below.

Respectfully submitted,

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In the Claims (Marked Version)

11. (three times amended) A method for preventing clotting in an extracorporeal blood circuit of a patient undergoing chronic, intermittent, extracorporeal blood treatment comprising administering for each treatment to the patient or to the circuit 0.001 to 10 mg of methyl O-(3,4-di-O-methyl-2,6-di-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(3-O-methyl-2-O-sulpho-ß-D-glucopyranosyl uronic acid)-(1→4)-O-(2,3,6-tri-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(3-O-methyl-2-O-sulpho-α-L-idopyranosyl uronic acid)-(1→4)-2,3,6-tri-O-sulpho-α-D-glucopyranoside or a salt thereof per kg body weight of the patient.

12. (three times amended) A method for preventing clotting in an extracorporeal blood circuit of a patient undergoing chronic, intermittent, extracorporeal blood treatment comprising administering for each treatment to the patient or to the circuit 0.30 to 30 mg of methyl O-(3,4-di-O-methyl-2,6-di-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(3-O-methyl-2-O-sulpho-ß-D-glucopyranosyl uronic acid)-(1→4)-O-(2,3,6-tri-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(3-O-methyl-2-O-sulpho-α-L-idopyranosyl uronic acid)-(1→4)-2,3,6-tri-O-sulpho-α-D-glucopyranoside or a salt thereof.

15. (three times amended) A method for preventing clotting in an extracorporeal blood circuit of a patient undergoing chronic, intermittent, extracorporeal blood treatment comprising administering for each treatment to the patient or to the circuit 0.001 to 10 mg of methyl O-(2,3,4-tri-O-methyl-6-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(2,3-di-O-methyl-ß-D-glucopyranosyl uronic acid)-(1→4)-O-(2,3,6-tri-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(2,3-di-O-methyl-α-L-idopyranosyl uronic acid)-(1→4)-2,3,6-tri-O-sulpho-α-D-glucopyranoside or a salt thereof per kg body weight of the patient.

16. (three times amended) A method for preventing clotting in an extracorporeal blood circuit of a patient undergoing chronic, intermittent, extracorporeal blood treatment comprising administering for each treatment to the patient or to the circuit 0.30 to 30 mg of a methyl O-(2,3,4-tri-O-methyl-6-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(2,3-di-O-methyl-ß-D-glucopyranosyl uronic acid)-(1→4)-O-(2,3,6-tri-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(2,3-di-O-methyl-α-L-idopyranosyl uronic acid)-(1→4)-2,3,6-tri-O-sulpho-α-D-glucopyranoside or a salt thereof.